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PATENT
Attorney's Docket No.: 033343-001

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:)
Harrington *et al.*) Group Art Unit: 1632
Serial No.: 09/276,820) Examiner: Shukla, R.
Filed: March 26, 1999)
For: COMPOSITIONS AND METHODS)
FOR NON-TARGETED ACTIVATION)
OF ENDOGENOUS GENES)

REQUEST BY APPLICANTS FOR INTERFERENCE
PURSUANT TO 37 C.F.R. § 1.607

Honorable Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

Claims 58-59, 64-69, 71-74, 76-82, 85-123, 128, 129, 131-132, 157, 159, 161, 162, 164-167, 169-175, 177-183, 223-226 and 232-270 of the present application have been canceled by an Examiner's amendment in favor of Claim 271, which was added to the application in Applicant's Second Supplemental Amendment filed on June 27, 2001. Claim 271 is now the only pending claim in the case.

Applicants Harrington *et al.* respectfully request, pursuant to 37 CFR § 1.607, that an interference be declared between the present application and U.S. Patent No. 6,080,576, which was issued to Zambrowicz *et al.* on June 27, 2000, a copy of which is attached as Appendix D.

The information required by 37 CFR § 1.607(a) is set forth below under headings which correspond to the subsections of § 1.607 to facilitate consideration by the Examiner.

I. IDENTIFICATION OF THE PATENT WHICH INCLUDES SUBJECT MATTER WHICH INTERFERES WITH THE PRESENT APPLICATION

U.S. Patent No. 6,080,576 ("the Zambrowicz '576 patent") claims subject matter which interferes with subject matter claimed in the present application ("the Harrington application"). The Zambrowicz '576 patent issued on application Serial No. 09/057,328, which was filed April 8, 1998, and claims priority from Provisional Application Serial No. 60/079,729, filed on March 27, 1998. The assignee named on the face of the patent is Lexicon Genetics Incorporated.

II. PRESENTATION OF A PROPOSED COUNT

Attached Appendix A sets forth a proposed count for the Examiner's consideration.

The language in the proposed count preceding the word -OR- is identical to the language of newly allowed Claim 271 of the present Harrington *et al.* application. The language following the word -OR- is identical to the language of Claim 15 of Zambrowicz.

III. THE PROPOSED COUNT INCLUDES THE DIFFERENT TERMS USED BY BOTH PARTIES TO DESCRIBE THE SAME INVENTION

Alternative counts are being proposed in part because of the different language utilized by the respective parties to describe the same invention.

A. ACTIVATE — ALTER

Claim 271 of the Harrington *et al.* application recites a method to "activate" expression of a gene; Claim 15 of the Zambrowicz '576 patent recites a method to "alter" expression of a gene. While the term "alter" is not specifically defined in the specification

of the '576 patent, numerous passages make it clear that the method of altering expression of a gene at least includes activating or over-expressing the gene. See for example, column 3, lines 8-10, where it is explained that one embodiment of the invention of the '576 patent is the use of the described vectors to activate gene expression.

B. VECTOR CONSTRUCT — 3' GENE TRAP CASSETTE VECTOR

Claim 271 of the present application recites introducing a vector construct into an isolated eukaryotic cell; Claim 15 of the Zambrowicz '576 patent recites introducing a 3' gene trap cassette vector. Both vectors are defined in the respective claims as comprising in operable combination 1) a promoter; 2) an exon sequence located 3' from and expressed by said promoter said exon being derived from a naturally occurring eukaryotic gene; and 3) a splice donor sequence defining the 3' region of said exon said splice donor sequence being derived from a naturally-occurring eukaryotic gene. Thus, the "vector construct" of Claim 271 and the "3' gene trap cassette vector" are synonymous terms.

C. SCREENABLE MARKER GENE — REPORTER GENE

Claim 15 of the Zambrowicz '576 patent specifies that the eukaryotic exon of the vector does not encode an activity conferring antibiotic resistance, and that it is not a reporter gene. As the Zambrowicz '576 patent specification states, given that the exon of the described 3' gene trap cassette of Claim 15 is comprised of sequence native to a eukaryotic cell, the exon will not constitute a marker that encodes a protein activity that provides an antibiotic resistance. See the Zambrowicz '576 patent at column 7, lines 31-39, and Claim 15. Since the antibiotic resistance, disclaimed in Claim 15, is prokaryotic, the claim term "said exon not encoding an activity conferring antibiotic resistance" does not

further limit Claim 15, and is therefore superfluous. Claim 271 of the Harrington application does not contain this superfluous limitation.

The Zambrowicz patent refers to a "reporter gene" as being a gene that mediates detection via conventional chromogenic or fluorescent assays, which are screenable. See the Zambrowicz '576 patent at column 7, lines 41-43. Claim 15 requires that said exon not be "a reporter gene."

Claim 271 of the Harrington *et al.* application specifies that the exon is not a screenable marker gene. Harrington *et al.* further specifies that a "screenable marker" is a gene that allows the cells containing the vector to be isolated without placing them under drug or other selective pressures. Examples are genes encoding cell surface proteins, fluorescent proteins, and enzymes. See the Harrington *et al.* application at page 28, lines 6-10. The term "reporter gene" used by Zambrowicz refers to the same marker genes that are referred to as "screenable markers" by Harrington *et al.*

D. ENDOGENOUS GENE — CELLULARLY ENCODED GENE

Harrington *et al.* teach that the vector construct can contain a screenable marker in place of a selectable marker, and that the selectable marker may be omitted from the vector construct. Harrington *et al.* application at page 25, line 30 to page 26, line 2; page 26, line 30 to page 27, line 2; and page 28, lines 14 to 16. Where the vector construct lacks a selectable/screenable marker, the exon will not encode a screenable marker. The claim limitations "and not being a screenable marker gene" of Harrington *et al.* Claim 271 and "and said exon not being a reporter gene" of the Zambrowicz '575 patent Claim 15 are believed to be synonymous.

Claim 15 of the Zambrowicz '576 patent refers to a splice acceptor sequence of "said cellularly encoded gene." Claim 271 of the Harrington *et al.* application refers to "said endogenous gene." Those of skill in this art readily recognize that a "cellularly encoded gene" is an "endogenous gene." At column 20, lines 31 to 35 of the '576 patent, Zambrowicz states that the 3' gene trap cassette can be used to mutagenize, activate or control the expression of "endogenous genes" in a wide variety of eukaryotic target cells. The terms "cellularly encoded genes" and "endogenous genes" are synonymous.

IV. IDENTIFICATION OF CLAIMS OF THE ZAMBROWICZ
PATENT WHICH CORRESPOND TO THE PROPOSED COUNT

The Zambrowicz '576 patent has 21 claims. To assist the Examiner, attached Appendix B sets forth a side-by-side comparison of Claim 271 of the Harrington *et al.* application with Claim 15 of the Zambrowicz patent. Claims 5-21 of the patent are also believed to correspond to the proposed count. Claims 5 and 6 are directed to genetically engineered vectors which contain a 3' gene trap cassette having in operable combination a promoter, an exon sequence and a splice donor sequence defining the 3' region of the exon that are identical to those specified for use in the method of Claim 15. These vectors are believed to be obvious in view of the method of Claim 15 of Zambrowicz and Claim 271 of Harrington *et al.*, and in view of the proposed Count.

Claims 7 to 14 are directed to methods of gene trapping in which one of the vectors of at least Claims 5 and 6 is introduced into an isolated eukaryotic target cell. These claims are likewise believed to be obvious in view of the method of the proposed Count. Claims 16 to 21, which depend from Claim 15, are likewise directed to methods which are believed to correspond to the proposed count.

V. CLAIM 271 OF THE HARRINGTON APPLICATION
CORRESPONDS TO THE PROPOSED COUNT

Claim 271 of Harrington *et al.* corresponds identically to the portion of the count preceding the word — OR — to the proposed count. To assist the Examiner, Applicants attach Appendix C. Appendix C is a chart providing an element-by-element recitation of newly allowed Claim 271 of Harrington *et al.* and an indication of the passages in the originally filed application where, at the very least, the claims find exemplary support.¹

VI. 35 U.S.C. § 135(b) IS SATISFIED

Claim 271, the only pending claim of the present application was submitted in a paper filed on June 27, 2001, within one year from the date the Zambrowicz '576 patent issued. It is respectfully submitted that the requirement of 35 U.S.C. 135(b) is satisfied.

VII. HARRINGTON *ET AL.* SHOULD BE DESIGNATED AS SENIOR PARTY

The present Harrington *et al.* application is the latest in a chain of continuation-in-part applications which include Serial No. 08/941,223, filed September 26, 1997, Serial No. 09/159,643, filed September 24, 1998, Serial No. 09/253,022, filed February 19, 1999, and Serial No. 09/263,814, filed March 8, 1999, all now abandoned. Support for the proposed count found in each of these applications is identified in Appendices C1-C5 respectively. Accordingly, Harrington *et al.* should be accorded benefit of these prior applications in the declaration of interference. Harrington *et al.* should also be designated as the senior party in the interference as having the earlier effective filing date, *i.e.*, September 26, 1997, versus at the earliest, March 27, 1998, for Zambrowicz.

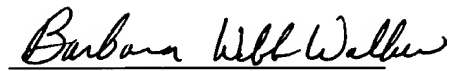
¹ Applicants reserve the right to identify and demonstrate additional support if necessary or desirable.

VIII. CONCLUSION

Applicants respectfully request that an interference be declared employing the proposed count set forth on attached Appendix A with Claim 271 of the Harrington *et al.* application and that Claims 5-21 of the '576 Zambrowicz patent be designated as corresponding to the count.

Respectfully submitted,

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